

CLAIMS

1. A method of obtaining a specific binding pair (sbp)  
member that binds a complementary sbp member of interest, the  
5 method comprising:

(a) providing mRNA molecules, each mRNA molecule  
comprising a nucleotide sequence encoding a specific binding  
pair member and lacking an in-frame stop codon;

(b) incubating the mRNA molecules under conditions for  
10 ribosome translation of the mRNA molecules to produce encoded  
specific binding pair member, whereby complexes each  
comprising ribosome, mRNA and encoded specific binding pair  
member displayed on the ribosome are formed;

(c) bringing the complexes into contact with the  
15 complementary sbp member of interest, and selecting one or  
more complexes displaying specific binding pair member able to  
bind the complementary sbp member of interest under the  
conditions of the selection;

wherein the mRNA molecules are incubated with prokaryotic  
20 ribosomes in a prokaryotic ribosome display system or are  
incubated with eukaryotic ribosomes in a eukaryotic ribosome  
display system;

the method being characterised in that the mRNA molecules  
further comprise a sequence for encapsidation of the mRNA  
25 molecules in a viral coat, and the method comprises providing  
viral coat protein that recognises the sequence for  
encapsidation, thereby encapsidating complexes of mRNA,  
ribosome and displayed specific binding member in the viral  
coat protein.

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2. A method according to claim 1 wherein the mRNA molecules  
incorporate a Midvariant (MDV) RNA template enabling  
replication by Q $\beta$  replicase.

3. A method according to claim 1 wherein a gly-ser tether is fused C-terminally to specific binding pair member.

4. A method according to claim 3 wherein the gly-ser tether comprises 24 glycine-serine units.

5. A method according to claim 1 wherein oxidised and reduced glutathione is added at a ratio of between 1:1 and 10:1 after 30 minutes of ribosome translation.

6. A method according to claim 1 wherein protein disulphide isomerase (PDI) is employed in the incubation conditions, along with oxidised and reduced glutathione at a ratio of 1:1 and 10:1.

7. A method according to claim 1 wherein the translation system is eukaryotic and protein disulphide isomerase (PDI) is employed in the incubation conditions.

8. A method according to claim 1 comprising selecting for complexes comprising a specific binding member able to bind complementary specific binding member of interest, while blocking unspecific selection using heparin.

9. A method according to claim 1 wherein mRNA molecules for incubation in the translation system are provided by means of RT-PCR reactions in which at least one RT-PCR primer is a mutagenic primer encoding a diversity of different sequences for inclusion in a defined region of the nucleotide sequence encoding a specific binding pair member.

10. A method according to claim 1 wherein tobacco mosaic

virus (TMV) viral coat protein and sequence for encapsidation ("origin assembly sequence" - "OAS") are employed.

11. A method according to claim 1 further comprising  
5 retrieving mRNA from a complex selected in step (c).

12. A method according to claim 11 wherein mRNA retrieved from a selected complex displaying a specific binding pair member (a "selected specific binding pair member") is  
10 amplified and copied into DNA encoding the selected specific binding pair member.

13. A method according to claim 12 wherein the DNA is  
provided in an expression system for production of a product,  
15 which product is the selected specific binding pair member or  
a polypeptide chain of the selected specific binding pair  
member.

14. A method according to claim 13 further comprising  
20 isolating or purifying the product.

15. A method according to claim 14 further comprising formulating the product into a composition comprising at least one additional component.

16. A method according to claim 15 wherein DNA encoding the selected specific binding pair member or a polypeptide chain of the selected specific binding pair member is provided within a nucleotide sequence to provide a nucleotide sequence encoding a fusion protein comprising the selected specific binding pair member, or a polypeptide chain of the selected specific binding pair member, fused to additional amino acids.



24. A method according to claim 23 further comprising formulating the product into a composition comprising at least one additional component.

5 25. A nucleic acid construct which is DNA or RNA comprising the following elements: an RNA polymerase binding site, a Kozak consensus sequence, a ribosome binding site, an initiation codon, a coding sequence encoding a fusion protein comprising a polypeptide and a tether, the coding sequence  
10 lacking a termination codon, and a sequence for encapsidation of mRNA in a viral coat.

26. A library or population of RNA molecules in accordance with claim 25, each RNA molecule in the library or population  
15 containing a sequence encoding a specific binding pair member, wherein the library or population collectively encodes a population or repertoire of specific binding pair members of diverse sequence.

20 27. A library or population of RNA molecules according to claim 26 which is packaged within viral coat protein.

28. A population of viral particles collectively containing a population or library of RNA molecules according to claim 27.

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29. An expression system comprising a nucleic acid construct according to claim 25 under culture conditions for production of fusion protein comprising polypeptide and tether.

30 30. An expression system comprising a library or population according to claim 26 under culture conditions for production of fusion protein comprising polypeptide and tether.